REMARKS/ARGUMENTS

The Status of the Claims.

Claims 1 to 12 and 14 to 18 are pending with entry of this amendment, claims 13 and 19 to 25 being cancelled herein. Claims 1, 10 and 15 are amended herein. These amendments introduce no new matter and support is replete throughout the specification. These amendments are made without prejudice and are not to be construed as abandonment of the previously claimed subject matter or agreement with any objection or rejection of record.

With respect to claim1, the amendment merely includes sequence identification numbers for amino acid sequences of the original specification and claim.

With respect to claim 10, support for an isolated monoclonal antibody can be found throughout the specification. For example, see specification in the Summary of the Invention, Figures 1 to 4 and associated text, the "Monoclonal antibodies to CYP1B1"section at page 19, at page 8, line 30, and page 10, line 27.

With respect to claim 15, the claim dependency is merely changed without addition of subject matter.

Applicants submit that no new matter has been added to the application by way of the above Amendment. Accordingly, entry of the Amendment is respectfully requested.

The Election/Restriction Requirement.

Pursuant to a restriction requirement made final, Applicants cancel claims 19 to 25 with entry of this amendment. Please note, however, that Applicants reserve the right to file subsequent applications claiming the canceled subject matter and the claim cancellations should not be construed as abandonment or agreement with the Examiner's position in the Office Action.

Compliance with the Sequence Listing Rules.

The Action, at page 4, requests a sequence listing along with a statement according to CFR sections 1.825, et seq. Applicants note that such a sequence listing and statement have previously been filed on February 2, 2006. A PAIRS inquiry finds a record of this filing in the USPTO database. However, if the Office would like the sequence listing resubmitted, Applicants will be happy to comply on request.

The Information Disclosure Statement.

Applicants note with appreciation the Examiner's thorough consideration of the references cited in the Information Disclosure Statement (Form 1449) submitted on March 14, 2002.

35 U.S.C. § 101.

Claims 10 to 18 were rejected under 35 U.S.C. § 101, as allegedly failing to distinguish the claimed antibodies over naturally occurring products. However, with the amendment of claim 10 to further include clearly statutory subject matter of "isolated" antibody forms, the rejection becomes moot. Applicants respectfully request withdrawal of the section 101 rejections.

35 U.S.C. §102.

Claims 10 to 12 and 18 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Pottenger (Arch. Biochem. Biophys. 286:488; 1991). Applicants traverse.

In order for a reference to anticipate an invention, the reference must teach each and every element of the claimed invention. That is, in order for a reference to anticipate an invention, anticipation requires that "all limitations of the claim are found in the reference, or be 'fully met' by it." Kalman v. Kimberly-Clark Corp., 218 USPQ 781, 789 (Fed. Cir. 1983). Here, Pottenger fails to describe limitations of the claims and thus can not be considered to anticipate the claims.

"To serve as an anticipation when the reference is silent about the asserted inherent characteristic, such gap in the reference may be filled with recourse to extrinsic evidence. Such evidence must make clear that the missing descriptive matter is [1] necessarily present in the thing described in the reference, and that it would be so [2]

recognized by persons of ordinary skill." *Continental Can Co. USA v. Monsanto Co.*, 948 F.2d 1264, 1268, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991). Pottenger is said to describe preparation of a polyclonal antibody to a mouse P450 1B1 sequence. The rejection is based on the statement that "a polyclonal antibody generated using murine p450 would 'specifically bind' to that epitope, in addition to other ones found in the p450 protein." This is not necessarily the case, so the rejection should be withdrawn.

The preparation of polyclonal antibodies in a chicken or rabbit against a murine protein does not necessarily result in antibodies that bind all sequences of the protein. The raising of chicken or rabbit polyclonal antibodies against murine P450 does not inherently provide the antibodies of the invention for a variety of reasons. For example, a rabbit might not develop antibodies to amino acid sequences that are substantially similar to their own, i.e., sequences that do not appear "foreign" to the rabbit. The mouse peptide sequences of the claimed invention may be non-immunogenic to the chicken or rabbit. The sequences will not necessarily be immunogenic to the rabbit or chicken, e.g., if they are identical to the analogous rabbit or chicken sequences, nearly identical, not presented on the surface of the protein, or the like. Evidence from Pottenger itself supports this fact. In the Abstract, Pottenger acknowledges that rabbit and chicken polyclonal antibodies have substantial differences in binding and target inhibition that clearly confirm that the polyclonal antibodies raised to a protein do not always include antibodies to all sequences in the protein. Because the polyclonal antibodies of Pottenger do not necessarily include antibodies that recognize an epitope of p450 CYP1B1 protein included within the amino acid sequence VNQWSVNHDPVKWPN or PExFDPARFLDKDGy, Pottenger can not be considered to anticipate claim 10 or its associated dependent claims.

The present claims include additional limitations not described in Pottenger. Amended claim 10 is directed to "an isolated monoclonal antibody". Because Pottenger does not teach monoclonal antibodies recognizing epitopes in the cited amino acid sequences, further reasons exist that the claims are not anticipated by Pottenger. Because Pottenger does not expressly or inherently teach the antibodies of claim 10, Applicants respectfully request withdrawal of the rejection.

Because Pottenger does not anticipate independent claim 10, neither can it be considered to anticipate the associated dependent claims. Furthermore the more specific target epitope sequences of claims 11 and 12 only further enhance the argument that a polyclonal antibody preparation raised in the Pottenger chickens and rabbits would not necessarily include antibodies recognizing the specific epitopes of the claims.

With regard to claim 18 antibodies for medical treatment, because the antibodies are not necessarily specifically binding to the cited amino acid sequences, they would not necessarily have the same medical benefits or indications as the claimed antibodies. This, again, is confirmed in Pottenger itself, e.g., wherein chicken polyclonal antibody was effective at inhibiting DMBA metabolism, but the rabbit polyclonal antibody was not.

Claims 10 to 13 and 18 were rejected under 35 U.S.C. §102(b) as allegedly anticipated by Melvin et al., (WO 97/122460). Applicants traverse.

Melvin describes preparation of polyclonal antibodies against CYP1B1 in rabbits using oligopeptides specifically not those of the present claims (see page 9). Melvin mentions that polyclonal or monoclonal antibodies suitable for use [in immunohistochemistry assays for CYP1B1 antigen] can be obtained according to conventional procedures.

Melvin does not teach all the limitations of claim 10. With regard to the preparation of polyclonal antibodies, Applicants reiterate the arguments above presented with regard to the rejection for alleged anticipation by Pottenger. Applicants note that Western blot detection of CYP1B1 in Melvin using polyclonal antibodies raised against oligopeptides specifically not included in the present claims shows that polyclonal detections of CYP1B1 does not necessarily require the presence of antibodies specifically binding the sequences cited in claim 10. Applicants note the facts show that Melvin did not raise any polyclonal or monoclonal antibodies against the specific sequences of claim 10.

Because Melvin did not raise polyclonal or monoclonal antibodies to whole CYP1B1 or to the polypeptides cited in claim 10, the rejection can only hinge on the teaching at page 9 of Melvin, that methods exist in the universe to raise antibody preparations against CYP1B1. Such a rejection can not stand because this does not teach, or inherently teach,

e.g., an isolated monoclonal antibody that recognizes an epitope that binds to the specific amino acid sequences VNQWSVNHDPVKWPN or PExFDPARFLDKDGy, where x is D or N and y is L or F.

Applicants note that preparation of monoclonal antibodies to whole CYP1B1 does not necessarily provide the isolated monoclonal antibodies of claim 10, and therefore the claim is not anticipated by Melvin. Monoclonal antibodies are generally isolated by, e.g., exposing a mouse to an antigen of interest, harvesting activated B-lymphocytes from the spleen of the mouse, fusing the lymphocytes with immortal cells to form a hybridoma possibly expressing a single antibody to a single epitope of the antigen, screening the hybridomas for expression of an antibody of interest and cloning a hybridoma expressing an antibody of interest. Should one create monoclonal antibodies starting with the CYP1B1 sequences of Melvin, no antibody of claim 10 could possibly result. Should one create a monoclonal antibody starting with exposure of the mouse to full-length CYP1B1, a monoclonal antibody ultimately produced would not necessarily be directed to an epitope of the cited amino acid sequences. Therefore, Melvin can not be considered to anticipate the present claims according to the holding of *Continental Can Co.* For example, the monoclonal antibody produced would not be directed to the cited epitopes including the amino acid sequences of the claim if: 1) the cited sequences were not sufficiently immunogenic to the mouse (e.g., not "foreign" enough or not adequately presented on the CYP1B1 protein), 2) if B-lymphocytes of interest fail to fuse with the immortal cells to form viable hybridomas, 3) if the screening method for hybridoma clones was not specific for cells producing antibodies against the cited amino acid sequences or were unsuccessful (note - Melvin did not teach a specific clone screening method that would provide the claimed antibodies), and/or 4) if the hybridomas selected in the screening did not include the cited amino acid sequences or failed to grow in the cloning step. Any given monoclonal randomly raised against full length CYP1B1 would be unlikely to be specific to the cited amino acid sequences; and screening techniques to specifically select the cited sequences are not taught in the art. Typically, efforts to raise monoclonal antibodies to an antigen do not result in isolation of antibodies to epitopes including all sequences of an antigen. Monoclonal antibodies prepared against CYP1B1 would not inherently recognize any particular epitope

of CYP1B1, and certainly not inherently recognize epitopes of the sequences cited in claim 10. Therefore, the rejections for alleged anticipation based on Melvin must be withdrawn.

As with Pottenger, because Melvin does not anticipate independent claim 10, neither can it be considered to anticipate the associated dependent claims. Furthermore, the more specific target epitope sequences of claims 11 and 12 only further diminish the likelihood that in a given hybridoma clone would be found expressing a monoclonal antibody recognizing the cited amino acid sequences. With regard to claim 18 antibodies for medical treatment, because the antibodies are not necessarily specifically binding to the cited amino acid sequences, they would not necessarily have the same medical benefits or indications as the claimed antibodies.

Because Melvin does not teach isolated monoclonal antibodies recognizing epitopes of VNQWSVNHDPVKWPN or PExFDPARFLDKDGy, where x is D or N and y is L or F, Applicants respectfully request withdrawal of the section 102 rejections.

35 U.S.C. §103(a).

Claims 16-17 were rejected under 35 U.S.C. §103(a) as allegedly obvious based on Melvin in light of Chiocca et al., (US 5,688,773). Applicants traverse.

Three requirements must be met for a *prima facie* case of obviousness. First, the prior art reference must teach all of the limitations of the claims. M.P.E.P § 2143.03. Second, there must be a motivation to modify the reference or combine the teachings to produce the claimed invention. M.P.E.P. § 2143.01. Third, a reasonable expectation of success is required. M.P.E.P. § 2143.02. The teaching or suggestion to combine and the expectation of success must be both found in the prior art and not based on Applicants' disclosure. M.P.E.P. §2143.

Here, not all limitations of claims 16 and 17 are provided in the cited combination of references. For example, dependent claims include all the limitations of the claims upon which they are dependent. Melvin does not provide a monoclonal antibody recognizing an epitope in the cytochrome P450 CYP1B1 protein included within the amino acid sequence VNQWSVNHDPVKWPN or PExFDPARFLDKDGy, where x is D or N and y is L or F; and these limitations are not taught by Chiocca. Because the cited combination of references fails to provide all limitations of the claims, the rejection must be withdrawn.

Allowable Claims

Applicants appreciate that the Office has found claims 2 to 9 to be allowable, and claim 1 allowable with adjustment over an objection. In light of current amendments and arguments, Applicants look forward to a Notice of Allowance for all pending claims after consideration of this Response.

CONCLUSION

In view of the foregoing, Applicants believes all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the claims are deemed not to be in condition for allowance after consideration of this Response, a telephone interview with the Examiner is hereby requested. Please telephone the undersigned at (510) 337-7871 to schedule an interview.

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Respectfully submitted,

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Attachments:

1) A petition to extend the period of response for **2** months;
2) A transmittal sheet;
3) A fee transmittal sheet; and,
4) A receipt indication postcard.